Paper No. 18

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

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Ex parte GUIDO FRANCOIS, GERHARD BRINGMANN, DAVID J. PHILLIPSON, MICHAEL R. BOYD, LAURENT A. ASSI, and CHISTOPH SCHNEIDER

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Appeal No. 2001-1335
Application No. 08/843,582

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ON BRIEF

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Before GARRIS, OWENS, and PAWLIKOWSKI, Administrative Patent Judges.

GARRIS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on an appeal from the final rejection of claims 28-45 which are all of the claims remaining in the application.

The subject matter on appeal relates to a pharmaceutical composition of a pharmaceutically acceptable carrier and an

antimalarially effective amount of at least one compound selected from a group of particular arylisoquinoline compounds or derivatives thereof. The appealed subject matter also relates to a method of treating or preventing a malarial infection or of inhibiting the growth of a malarial parasite which comprises administering an antimalarially effective amount of at least one compound selected from the aforementioned group. This appealed subject matter is adequately illustrated by independent claims 28 and 34, a copy of which taken from the appellants' brief is appended to this decision.

The references relied on by the examiner in the section 102 and section 103 rejections before us are set forth below:

Sloan	5,001,115	Mar. 19, 1991
Bringmann et al. (Bringmann III)	5,260,315	Nov. 9, 1993

Ruangrungsi et al. (Ruangrungsi), "Traditional medicinal plants of Thailand, V. Ancistrotectorine, a new naphthaleneisoquinoline alkaloid from *ancistrocladus tectorius*," Journal of Natural Products, vol. 48, No. 4, pp. 529-535 (1985).

Bundgaard, "Design of prodrugs: Bioreversible derivatives for various functional groups and chemical entities," Design of Prodrugs, pp. 1-3, 10, 35-37 (1985).

Bringmann et al. (Bringmann V), "On the structure of the dioncophyllaceae alkaloids dioncophylline A ("triphyophylline") and '*O*-methyl-triphyophylline'," Tetrahedron Letters, Vol. 31, No. 5, pp. 639-642 (1990).

Bringmann et al. (Bringmann II), "Atrop-diastereomer separation by racemate resolution techniques: N-methyl-dioncophylline A and

its 7-epimer from *ancistrocladus abbreviatus,"* Phytochemistry, Vol. 30, No. 4, pp. 1307-1310 (1991).

Bringmann et al. (Bringmann I), "Ancistrobrevine B, the first naphthylisoquinoline alkaloid with a 5,8'coupling site, and related compounds from *ancistrocladus abbreviatus*," Phytochemistry, Vol. 31, No. 11, pp. 4011-4014 (1992).

Bringmann et al. (Bringmann IV), "Dioncophylline C from the roots of *triphyophyllum peltatum*, the first 5,1'-coupled dioncophyllaceae alkaloid," Phytochemistry, Vol. 31, No. 11, pp. 4019-4024 (1992).

Bringmann et al. (Bringmann VI), "A new atropisomeric dioncophyllline A derivative from *triphyophyllum peltatum*," Planta Med., 59 Supplemental Issue (1993).

Claim 28 stands rejected under 35 U.S.C. § 102(e) as being anticipated by Bringmann III.

Claims 28-33 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Bringmann I or Bringmann II or Bringmann IV in view of Sloan and Bundgaard, and claims 34-45 stand correspondingly rejected as being unpatentable over these references and further in view of Bringmann V and Bringmann VI and Ruangrungsi.

We refer to the brief and to the answer for a complete exposition of the opposing viewpoints expressed by the appellants and by the examiner concerning the above noted rejections.

OPINION

For the reasons which follow, we cannot sustain any of the rejections advanced by the examiner on this appeal.

Regarding the section 102 rejection of composition claim 28, the examiner states that "the instantly claimed composition is anticipated by Bringmann's aqueous formulation comprising 0.05% dioncophylline B and water (column 4, lines 10-13), which is also a pharmaceutically acceptable carrier" (answer, page 4). We cannot agree for at least two reasons. First, it is not at all clear that Bringmann's aqueous formulation (i.e., the formulation of patentee's Example 1) constitutes a pharmaceutical composition of at least one pharmaceutically acceptable carrier as required by the claim under review. This is because, contrary to the examiner's apparent belief, this formulation does not comprise only dioncophylline B and water. It also includes at least one other ingredient, namely, an emulsifier (e.g., see line 56 in column 3). For all we know, this additional ingredient may be contrary to a pharmaceutical composition having at least one pharmaceutically acceptable carrier as required by the here rejected claim. Thus, the examiner necessarily has implicitly assumed that Bringmann's formulation comprises the appellant's claimed pharmaceutical composition having at least one pharmaceutically acceptable carrier.

Additionally, the examiner necessarily has implicitly assumed that Bringmann's formulation satisfies the antimalarially

effective amount limitation of appealed claim 28. In this regard, the examiner urges that "the 0.05% of dioncophylline B in the aqueous formulation (column 4, lines 10-13) would fall within the effective range of the instant antimalarial composition for a dosage of 0.01 mg/kg body weight to 100 mg/kg body weight (page 32 of the specification)" (answer, page 8). However, there is absolutely no basis for the examiner's belief that patentee's disclosure of 0.05% dioncophylline B would fall within the range of antimalarially effective amounts disclosed by the appellants on page 32 of their specification. In fact, it is clear that Bringmann's 0.05% value relates to the concentration of dioncophylline B in his formulation and not to the total amount of the dioncophylline B present in the formulation. It is this total amount which must be known in order to assess whether it corresponds to the amounts disclosed by appellants as being antimalarially effective. Our study of Bringmann's Example 1 disclosure reveals that it is impossible to know the total amount of dioncophylline B which was present in the Example 1 formulation.

In light of the foregoing, it is apparent that the examiner's anticipation position is based on assumption and conjecture. It is well settled that anticipation under section

102 cannot be predicated on conjecture. W.L. Gore & Assocs. v. Garlock, Inc., 721 F.2d 1540, 1554, 220 USPQ 303, 314 (Fed. Cir. 1983); Ex parte Standish, 10 USPQ2d 1454, 1457 (Bd. Pat. App. Int. 1988). It follows that the section 102 rejection of claim 28 as being anticipated by Bringmann III cannot be sustained.

Regarding the section 103 rejections, we agree with the appellants that the Bringmann I, Bringmann II and Bringmann IV references contain no teaching or suggestion that the compounds disclosed therein possess any kind of pharmaceutical activity much less an antimalarial activity and therefore would not have suggested a pharmaceutical composition which contains an antimalarially effective amount of at least one compound of the types here under consideration as required by appealed claims 28-33. According to the examiner, "[s]ince it is known that all these compounds (Bringmann I, II, IV) are natural products derived from plants traditionally used for treating malaria, it is [sic, would have been] obvious for one of ordinary skill in the art to identify, extract and purify the active ingredients from the antimalarial plants and prepare the anti-malarial composition to arrive at the instant [i.e., the here claimed composition]" (answer, page 9). The examiner's position is not well taken for a number of reasons.

First, the Bringmann I, Bringmann II and Bringmann IV references do not disclose that the compounds described therein are derived from plants which are "traditionally used for treating malaria" (id.). While other references such as Bringmann V and Ruangrungsi may contain such disclosure, these references have not been applied against composition claims 28-33.[1] For this reason alone, the examiner's position concerning, and her concomitant rejection of, composition claims 28-33 are without merit.

Additionally, this position is unpersuasive with respect to method claims 34-45 which have been rejected over references that include Bringmann V and Ruangrungsi. This is because a prima facie case of obviousness is not established by the mere fact that the compounds under consideration are derived from plants

[1] We observe that Bringmann V and Ruangrungsi, like the Bringmann I, Bringmann II and Bringmann IV references, disclose compounds of the type defined by the appealed composition claims. However, unlike the Bringmann I, Bringmann II and Bringmann IV references, Bringmann V and Ruangrungsi also disclose that these compounds are derived from plants used in folk medicine for treating, for example, malaria. In light of these more comprehensive disclosures, it is unclear why the examiner did not rely upon Bringmann V and Ruangrungsi (rather than Bringmann I, Bringmann II and Bringmann IV) as primary references in her section 103 rejections. While such reliance would not have resulted in sustainable rejections as discussed more fully in the body of our decision, the examiner's above quoted position would have been, at least arguably, rational and germane with respect to composition claims 28-33.

used in folk medicine for treating, for example, malaria. In this regard, we point to the Boyd declaration under 37 CFR § 1.132 of record which evinces, inter alia, that "[t]he vast majority of compounds isolated from plants purportedly used in folk medicine do not exhibit the biological activity associated with the medicinal application for which the plant is purportedly used in folk medicine" and that, "[i]ndeed, the vast majority of compounds isolated from plants, including plants purportedly used in folk medicine, do not exhibit any biological activity whatsoever when subjected to biological screening" (item 8). Particularly in view of this declaration evidence, it is apparent that the examiner's conclusion of obviousness is inappropriately based upon an "obvious to try" standard which is not the proper standard under section 103. In re O'Farrell, 853 F.2d 894, 904, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988). Stated otherwise, the prior art applied by the examiner, including the Bringmann V and Ruangrungsi references, contain nothing which would have given an artisan with ordinary skill a reasonable basis for expecting the compounds under consideration would be successful for treating malaria. Id.

Under these circumstances, we also cannot sustain the examiner's section 103 rejection of claims 28-33 as being

unpatentable over Bringmann I or Bringmann II or Bringmann IV in view of Sloan and Bundgaard or the corresponding section 103 rejection of claims 34-45 as being unpatentable over these references and further in view of Bringmann V and Bringmann VI and Ruangrungsi.

The decision of the examiner is reversed.

REVERSED

Bradley R. Garris Administrative Patent Judge	)	
Terry J. Owens Administrative Patent Judge	)	BOARD OF PATENT APPEALS AND INTERFERENCES
Beverly A. Pawlikowski Administrative Patent Judge	)	

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APPENDIX

28. A pharmaceutical composition consisting essentially of at least one pharmaceutically acceptable carrier and an antimalarially effective amount of at least one compound selected from the group consisting of dioncophylline B, dioncopeltine A, dioncophylline A, dioncophylline C, ancistrobrevine D, ancistrocladine, *N*-methyl-dioncophylline A and the atropisomer thereof, dioncophylleine A, (±) - dioncophyllacine A, hamatine, ancistrobrevine B, ancistrobrevine A, 6-*O*-demethyl-ancistrobrevine A, ancistrobarterine A, 7-*epi*-dioncophylline A, *N*-formyl-ancistrocladine, *N*-methyl-ancistrocladine, 6-deoxy-*N*-methyl-ancistrocladine, *N*-formyl-*O*,*O*-dimethyl-dioncophylline C, *N*-formyl-dioncophylline C, *N*-formyl-8-*O*-benzyl-dioncophylline C, *N*-formyl-8-*O*-methyl-dioncophylline C, *N*-formyl-8-*O*-pivaloyl-dioncophylline C, *N*-formyl-8-*O*-acetyl-dioncophylline C, *N*-formyl-8-*O*-benzoyl-dioncophylline C, and 8-*O*-methyl-dioncophylline C, and pharmacologically acceptable salts thereof, optionally in combination with an antimalarially effective amount of at least one additional antimalarial compound selected from the group consisting of chloroquine, mefloquine, halofantrine, artemisinin, artemether, pyrimethamine, and quinine.

34. A method of treating or preventing a malarial infection which comprises administering to a mammal in need thereof an antimalarially effective amount of at least one compound selected from the group consisting of dioncophylline B, dioncopeltine A, dioncophylline A, dioncophylline C, ancistrobrevine D, ancistrocladine, *N*-methyl-dioncophylline A and atropisomer thereof, dioncophylleine A, (±) - dioncophyllacine A, hamatine, ancistrobrevine B, ancistrobrevine A, 6-*O*-demethyl-ancistrobrevine A, ancistrobarterine A, 7-*epi*-dioncophylline A, *N*-formyl-ancistrocladine, *N*-methyl-ancistrocladine, 6-deoxy-*N*-methyl-ancistrocladine, *N*-formyl-*O*,*O*-dimethyl-dioncophylline C, *N*-formyl-dioncophylline C, *N*-formyl-8-*O*-benzyl-dioncophylline C, *N*-formyl-8-*O*-methyl-dioncophylline C, *N*-formyl-8-*O*-pivaloyl-dioncophylline C, *N*-formyl-8-*O*-acetyl-dioncophylline C, *N*-formyl-8-*O*-benzoyl-dioncophylline C, and 8-*O*-methyl-dioncophylline C, and pharmacologically acceptable salts thereof.